IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Examiner: C.E. Simmons
Bond	)	Group Art Unit: 1612
Serial No.: 10/574,429	)	Docket No.: 8077-005-US
Filed: April 3, 2006	)	Date Transmitted: March 21, 2008
For: METHODS FOR TREATING DISEASES AND CONDITIONS WITH INVERSE AGONISTS AND FOR SCREENING FOR AGENTS ACTING AS INVERSE AGONISTS	)	

RESPONSE TO RESTRICTION REQUIREMENT AND REQUIREMENT FOR ELECTION OF SPECIES

Mail Stop: Amendment
Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicant responds to the Restriction Requirement and Requirement for Election of Species as follows:

I. THE RESTRICTION REQUIREMENT

The Examiner has stated that this application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1:

Group I is claims 1-3, 7-14, 19-20, and 37-41, drawn to a method for treating a disease or condition comprising administering an inverse agonist for the G protein coupled receptors (GPCR) that causes an increase in the population of GPCRs.

Group II is claims 42, 48, and 49, drawn to a method of screening comprising the steps of providing a population of specific GPCR, contacting the cells with compound, and determining the constitutive basal level of activity of the GPCRs in the absence and presence of the compound.

Group III is claim 52, drawn to a method of screening comprising the steps of providing a population of specific GPCR, contacting the cells with compound, and determining the receptor population or receptor density of the GPCRs in the cell in the absence of the compound and in the presence of the compound.

Group IV is claim 55, drawn to a method for treating a disease or condition associated with the activity of GPCR comprising administering an inverse agonist for the GPCR that prevents the decrease in the population of GPCRs.

Group V is claim 60, drawn to a composition.

The Restriction Requirement stated that the inventions listed as Groups I-V did not related to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features for the following reasons: The

common technical feature (i.e., a composition comprising an inverse agonist for a G-protein coupled receptor (GPCR) is taught in the prior art. Therefore, according to the Restriction Requirement, the common technical feature was not a special technical feature, *a posteriori*, when the teachings of United States Patent No. 4,402,976 to Muir ("Muir '976") are considered.

II. RESPONSE TO THE RESTRICTION REQUIREMENT

In response to the Restriction Requirement, Applicant elects the invention of Group I, claims 1-3, 7-14, 19-20, and 37-41, drawn to a method for treating a disease or condition comprising administering an inverse agonist for the G protein coupled receptors (GPCR) that causes an increase in the population of GPCRs, with traverse.

The Restriction Requirement is traversed on the following grounds:

Firstly, the reference cited in the Restriction Requirement, namely Muir '976, fails to disclose or suggest the special technical feature recited in claim 1, as amended herein. This special technical feature is the method for treating a disease or condition associated with the activity of a G protein coupled receptor (GPCR) comprising administering an inverse agonist for the GPCR to an organism with a disease or condition associated with the activity of the GPCR in a quantity and for a period that causes an increase in the population of GPCRs, either spontaneously active or those that are available and activated by an endogenous agonist or by an exogenous agonist, associated with that physiological function, thereby producing a therapeutic effect to ameliorate the disease or condition, recited in claim 1. Specifically, this method requires the administration of the inverse agonist in a quantity and for a period that causes the recited increase in the population of GPCRs.

Muir '976, although reciting a composition including nadolol, fails to recite that nadolol or any other inverse agonist, is administered in a quantity or for a period that would cause the required increase in the population of GPCRs. In fact, there is no information at all

provided in Muir '976 that provides any guidance or information as to the dosage required to induce inverse agonism at any GPCR or the period of administration required to cause the required increase in the population of any GPCR. Although dosages and frequencies of administration are provided, there is no information whatsoever about the duration or period of administration that is required to cause the required increase in the population of GPCRs. This constitutes the special technical feature of these claims, and Muir '976 fails to teach it.

Therefore, the special technical feature described above is not taught or suggested by Muir '976.

Accordingly, Applicant asserts that all pending claims do possess a special technical feature in common that is not disclosed or suggested by the prior art. Accordingly, the Examiner is respectfully requested to withdraw the Restriction Requirement.

In addition, the Restriction Requirement is traversed on the following grounds:

Firstly, the Examiner has not met the burden for demonstrating the necessity for restriction. M.P.E.P. § 803 requires for restriction both: (1) that the inventions are independent or distinct as claimed; and (2) that there would exist a "serious burden" on the Examiner if all of the claims were examined in one application. These requirements have not been met.

In fact, the subject matter of Groups I through V, claims 1-3, 7-14, 19-20, 37-41, 42, 48, 49, 55, and 60 are sufficiently related to avoid restriction, because there would be no "serious burden" on the Examiner if all of the claims were examined together in one application. The essence of the invention, from the standpoint of the imposition of a restriction requirement, is the discovery that inverse agonists can be used to cause an increase in the population of GPCRs and thus to treat diseases and conditions associated with the activity of GPCRs as recited in claim 1, and other claims merely express various aspects of this discovery, including screening methods and compositions for treating such diseases and conditions.

Accordingly, the subject matter of the invention is sufficiently interrelated that no serious burden on the Examiner would exist if all the claims were examined on the merits. That is because the relevant art involved, if any relevant art exists, largely overlaps for these claims. For example, any publications, patents, or published patent applications describing inverse agonism will typically set forth the conditions under which the agents displaying inverse agonism must be administered to display this activity. This statement is not to be taken as an admission that any such prior art exists, merely a statement that, should any relevant art exists, it is likely to be relevant to the subject matter of more than one group of claims. It is well known that inverse agonism is closely associated with the affinity of the agent for the receptor and thus is dependent on the dosage, dosage frequency, and period of administration.

Therefore, there is no basis for restriction of the claims based on the existence of a "serious burden" to the Examiner that would exist if the subject matter of all claims were examined on the merits.

Applicants do not traverse the Restriction Requirement on the grounds of lack of patentable distinctness. Rather, Applicants traverse the Restriction Requirement on the grounds that the inventions of Groups I through V are sufficiently related that restriction is not properly required, despite the possible existence of patentable distinctness.

Therefore, the Restriction Requirement is respectfully traversed and the Examiner is respectfully requested to withdraw the Restriction Requirement and to allow the examination of all of Groups I through V on the merits. In the event that the Restriction Requirement is not withdrawn, Applicant respectfully suggests, in the alternative, that the inventions of Groups I and IV, as method of treatment claims, be examined on the merits.

III. THE REQUIREMENT FOR ELECTION OF SPECIES

The Examiner has considered that this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

If Group I is elected with respect to the restriction requirement, the following elections of species must be made: (1) a single disclosed disease or condition for the specification or the claims (e.g., congestive heart failure in claim 37); (2) a single disclosed inverse agonist for the GPCR (e.g., nadolol, carazolol, etc. in claim 10; (3) whether an additional agent is present; if so, Applicant must further elect a single disclosed additional agent, e.g., albuterol, bitolterol, clenbuterol, clorprenaline, salbutamol, etc.); (4) a single disclosed GPCR (e.g., β_3-adrenergic receptors, dopamine receptors, etc.); (5) whether the composition further comprises an agonist to the GPCR if an additional agonist is present.

If Group II is elected with respect to the restriction requirement, the following elections of species must be made: (1) a single disclosed inverse agonist for the GPCR (e.g., nadolol, carazolol, etc. in paragraph **[0021]** of the specification; and (2) a single disclosed GPCR (e.g., β_3-adrenergic receptors, dopamine receptors, etc., in paragraph **[0024]** of the specification.

If Group III is elected with respect to the restriction requirement, the following elections of species must be made: (1) a single disclosed inverse agonist for the GPCR (e.g., nadolol, carazolol, etc. in paragraph **[0021]** of the specification; and (2) a single disclosed GPCR (e.g., β_3-adrenergic receptors, dopamine receptors, etc., in paragraph **[0024]** of the specification.

If Group IV is elected with respect to the restriction requirement, the following elections of species must be made: (1) a single disclosed disease or condition for the specification or the claims (e.g., congestive heart failure, obesity, etc. in paragraph **[0007]** of the specification); (2) a single disclosed inverse agonist for the GPCR (e.g., nadolol, carazolol, etc. in paragraph **[0021]** of the specification; and (3) a single disclosed GPCR (e.g., β_3-adrenergic receptors, dopamine receptors, etc., in paragraph **[0024]** of the specification.

If Group V is elected with respect to the restriction requirement, the following elections of species must be made: (1) a single disclosed inverse agonist for the GPCR (e.g., nadolol, carazolol, etc. in paragraph **[0021]**; and (2) a single disclosed second agent e.g., albuterol, bitolterol, clenbuterol, clorprenaline, salbutamol, etc., in the specification at paragraphs **[0162]** and **[0170]**).

Applicant is required, in reply to the Requirement for Election of Species, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added.

Upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. The Requirement for Election of Species indicated that the following claims are generic: claims 1, 42, 52, 55, and 60. However, other claims are generic with respect to one or more of the alternative species described above.

IV. RESPONSE TO THE REQUIREMENT FOR ELECTION OF SPECIES

In response to the Requirement for Election of Species, consistent with the election of Group I, the following elections are made:

(1) The single disclosed disease or condition is congestive heart failure.

(2) The single disclosed inverse agonist for the GPCR is nadolol.

(3) The additional agent is not present.

(4) The single disclosed GPCR is β_2-adrenergic receptors.

(5) The composition does not disclose an additional agonist to the GPCR.

These species read on the following claims:

(1) Congestive heart failure reads on the following claims: claims 1, 2. 37, 38, 39, 40, and 41. Of these claims, claims 1, 2, 40, and 41 are generic with respect to the species congestive heart failure in that they encompass additional diseases or conditions.

(2) Nadolol as the inverse agonist reads on the following claims: 1, 2, 3, 7, 8, 9, 10, 11, 12, 19, 20, 37, 38, 39, 40, 41, and 60. Of these, claims 1, 2, 3, 7, 8, 9, 10, 11, 12, 19, 20, 37, 38, 40, 41, and 60 are generic with respect to the species nadolol in that they encompass additional inverse agonists.

(3) The absence of the additional agent reads on the following claims: 1, 2, 3, 7, 8, 9, 10, 11, 12, 13, 14, 37, 38, 39, 40, and 41. All these claims are generic with respect to the species defined as the absence of the additional agent, as these claims encompass both methods using the additional agent and methods without the additional agent.

(4) The β_2-adrenergic receptor as the receptor reads on the following claims: 1, 2, 3, 7, 8, 9, 10, 11, 12, 13, 14, 19, 20, 37, 38, 39, and 60. Of these, claims 1, 2, 3, 19, 20, 37, and 60 are generic with respect to the species defined as the β_2-adrenergic receptor, as these claims encompass both methods or compositions in which the receptor is the β_2-adrenergic receptor and methods or compositions in which the receptor is other than the β_2-adrenergic receptor.

(5) The absence of the additional agonist to the GPCR reads on the following claims: 1, 2, 3, 7, 8, 9, 10, 11, 12, 13, 14, 19, 20, 37, 38, 39, 40, and 60. All these claims are

generic with respect to the species defined as the absence of the additional agonist, as these claims encompass both methods using the additional agonist and methods without the additional agonist. Please note that the "additional agent" of (3) and the "additional agonist" of (5) are different and define different species.

The Requirement for Election of Species is traversed on substantially the same grounds as the Restriction Requirement. That is, the reference relied upon, namely Muir '976, does not teach or suggest the special technical feature of any of these claims. As emphasized above, that special technical feature is the method for treating a disease or condition associated with the activity of a G protein coupled receptor (GPCR) comprising administering an inverse agonist for the GPCR to an organism with a disease or condition associated with the activity of the GPCR in a quantity and for a period that causes an increase in the population of GPCRs, either spontaneously active or those that are available and activated by an endogenous agonist or by an exogenous agonist, associated with that physiological function, thereby producing a therapeutic effect to ameliorate the disease or condition. This is not taught or suggested by Muir '976, as fully described above.

As with the Restriction Requirement, Applicants do not traverse the Requirement for Election of Species on the grounds of lack of patentable distinctness. Rather, Applicants traverse the Requirement for Election of Species on the grounds that the species described above, in the context of the overall invention, are sufficiently related that restriction is not properly required, despite the possible existence of patentable distinctness.

Additionally, it is submitted that the generic claims, including claims 1, 42, 52, 55, and 60, as well as the additional generic claims described above with regard to particular species, are allowable.

Therefore, the Requirement for Election of Species is respectfully traversed. This traversal applies whether or not the Restriction Requirement is withdrawn or not; if the Restriction Requirement is in fact withdrawn, the Requirement for Election of Species is

respectfully traversed with respect to the inventions of Groups I, II, III, IV, and V and with respect to all claims within those groups.

V. POSSIBLE REJOINDER

The Examiner has requested rejoinder between product and process claims. Where Applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all of the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R. § 1.104.

VI. CONCLUSION

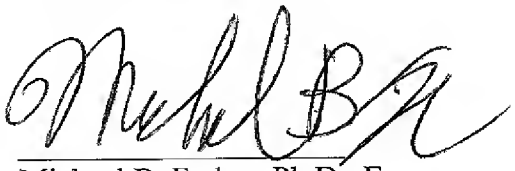
In conclusion, Applicant elects the invention of Group I, claims 1-3, 7-14, 19-20, and 37-41, drawn to a method for treating a disease or condition comprising administering an inverse agonist for the G protein coupled receptors (GPCR) that causes an increase in the population of GPCRs, for prosecution on the merits, with traverse.

With respect to the Requirement for Election of Species, Applicant elects the following species as applicable to the claims of Group I: (1) the single disclosed disease or condition is congestive heart failure; (2) the single disclosed inverse agonist for the GPCR is nadolol; (3) the additional agent is not present; (4) the single disclosed GPCR is β_2-adrenergic receptors; and (5) the composition does not disclose an additional agonist to the GPCR.

Applicant respectfully requests that the Restriction Requirement and the Requirement for Election of Species be withdrawn. In the event that the Restriction Requirement is not withdrawn, Applicant respectfully suggests, in the alternative, that the inventions of Groups I and IV, as method of treatment claims, be examined on the merits.

If any issues remain, the Examiner is respectfully requested to telephone the undersigned at (858) 450-0099 x302.

Respectfully submitted,



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Michael B. Farber, Ph.D., Esq.
Reg. No.: 32,612

CATALYST LAW GROUP, APC
9710 Scranton Road, Suite 170
San Diego, California 92121
(858) 450-0099
(858) 450-9834 (Fax)